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The Pattern of Cellular Organization of Human Epidermis

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Cell alignment in the stratum corneum of frozen sections of specimens of human skin was examined by light microscopy following expansion of the stratum corneum in alkaline buffer. Some degree of ordered structure was found in all specimens examined but considerable variation existed in precision of cell alignment. The typical degree of cell alignment was less precise than that typically observed in experimental animals.

Studies of the epidermis of rodents, carnivors, primates and birds [1-7] have shown that cells within the stratum corneum of the greater part of the epidermis are aligned to form columnar units of structure. Reports of observations made on human material suggest a comparable pattern in man but are limited in number [2,4,5]. To examine the degree of organization typical of human skin, a range of human specimens systematically collected from sites expected to show columnar organization was examined by standardized methods.

MATERIALS AND METHODS

Specimens of skin from 10 subjects ranging in age from 3 days to 71 yr were collected during postmortem examination from the midline of the abdomen and chest, from the posterior part of the scalp and from the inner surface of the upper arm. A full medical history was available for each subject examined. Specimens were trimmed to remove subcutaneous fat, oriented on plastic cover slips for sectioning perpendicular to the epithelial surface, mounted on cork discs [8], and frozen in isopentane cooled in liquid nitrogen. Frozen sections were cut at 8 μm, picked up on cover slips, fixed overnight in 1% acetic acid in 70% ethanol, stained in filtered 0.1% methylene blue and expanded in half strength Sorenson-Walbum buffer [9] at pH 12.0-12.5. Comparable areas of skin from adult rhesus monkeys, and ear and body skin from rodents was similarly prepared and examined. Five or more photographs taken of each human specimen, using a ×40 oil immersion objective lens, were printed at standard magnification and assessed for the pattern of organization within the tissue. The areas photographed were selected for the quality of histological preparation without regard to the structure of the stratum corneum. To provide a measure of comparison between specimens, the degree of organization visible in the stratum corneum and stratum granulosum of each photograph was graded on a scale of 1-3. The grading criteria used were:

Stratum Corneum

1. No evidence of a tendency towards alignment of cells within the stratum corneum.
2. A tendency towards a columnar pattern of cell alignment but with irregularities of cell interdigitation and without columns passing through the full sectioned thickness of the stratum corneum.
3. A more regular columnar pattern of alignment with individual columns traceable through the full thickness of the stratum corneum.

Stratum Granulosum

1. No distinguishable alignment of granular cells beneath cell columns in the stratum corneum.
2. Alignment of stratum granulosum cells occasionally visible beneath overlying stratum corneum cells.
3. One or more layers of granular cells often seen to be aligned beneath cell columns in the stratum corneum.

RESULTS

Specimens of human epidermis in comparison with specimens of rodent and rhesus monkey were found to be more difficult to process for expansion and the degree of expansion so produced was generally limited. All of the human specimens examined showed some evidence of a columnar pattern of organization in the stratum corneum but variation was found in the degree of order from specimen to specimen and within the same specimen. The range in the pattern of organization observed is illustrated in Fig 1 and 2. Even those specimens showing the greatest degree of ordering of the stratum corneum (Fig 1*A*) did not show a degree of alignment of cells as precise as that typically observed in rodent or rhesus epidermis (Fig 3) and the degree of overlap between the cells of adjacent columns was somewhat more variable. An appearance typical of the majority of the human specimens examined is shown in Fig 1*B*: nonrandomness of the position of cells in the stratum corneum is clearly seen but, although stacks of cells can be traced through the full thickness of the sectioned stratum corneum, individual cells interdigitate somewhat erratically with cells of the neighboring columns. Judged by the varying width and angle of the boundaries between the cut sections of columns, their vertical alignment was not precise. Figure 2*A* shows a specimen representing the least appearance of ordered structure observed: the degree of overlap between cells is quite extensive, but the tendency towards cell alignment is still apparent.

It was usually difficult to detect a clear alignment of stratum granulosum cells even where cell columns in the stratum corneum were well defined (Fig 1). Alignment of 2-3 layers of nucleated cells beneath the cell columns of the stratum corneum is typically seen in rodent epidermis but was only occasionally observed in human specimens (Fig 2*B*).

The results of grading the degree of organization of the stratum corneum and subjacent cells in each of the human specimens examined are shown in the Table. Within the limits imposed by the ordinal nature of the grading criteria, and by the number of specimens examined, summation of the grades for appropriate groups of specimens permitted a comparison of groups of data. No consistent distinctions could be drawn in terms of a more or less regular cell alignment with regard to the four anatomical regions examined, or with age or sex.

DISCUSSION

Previous studies [4,5] have demonstrated the existence of a columnar pattern of organization in specimens of human skin but have not systemically examined a sufficient range of subjects, or range of sites within each subject, to establish what may be considered to be the typical degree of organization present in man or to permit a comparison of the pattern of human organization with that of other species. In the epidermis of rodents and the rhesus monkey [1-7, 10] a columnar pattern of organization has been found present in most regions of the epidermis except specialized regions such as plantar and palmar surfaces and the region of the nipple (and also the oral mucosa) where the surface epithelia are generally thicker [11]. A similar absence of a columnar pattern in the stratum corneum of

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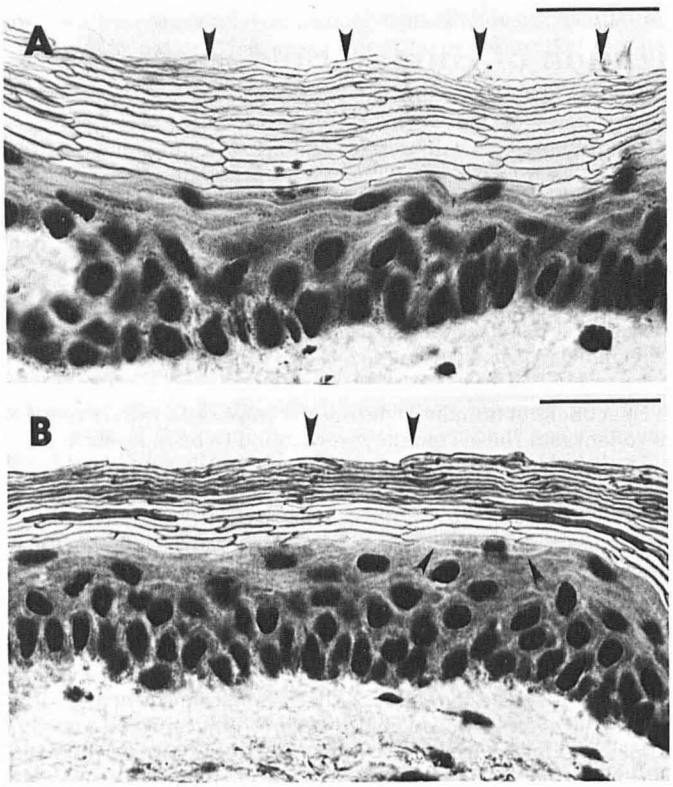

FIG 1. *A*, Specimen illustrating the most regular alignment of stratum corneum cells observed. Cell columns pass vertically through the full thickness of the sectioned stratum corneum but cells of adjacent columns interdigitate irregularly. Alignment of granular cells is not frequently observed. Abdominal skin from 67-yr-old female. *B*, Specimen illustrating the typical degree of alignment observed in human epidermis. Cell alignment is apparent and, in areas, columns can be traced vertically through the full sectioned thickness of the stratum corneum (*arrows*). In other areas cut segments of columns are seen or columns run at an oblique angle. *Smaller arrows* indicate alignment of a granular cell. Skin from inner surface of arm of 32-yr-old male (*scale* = 30 μm).

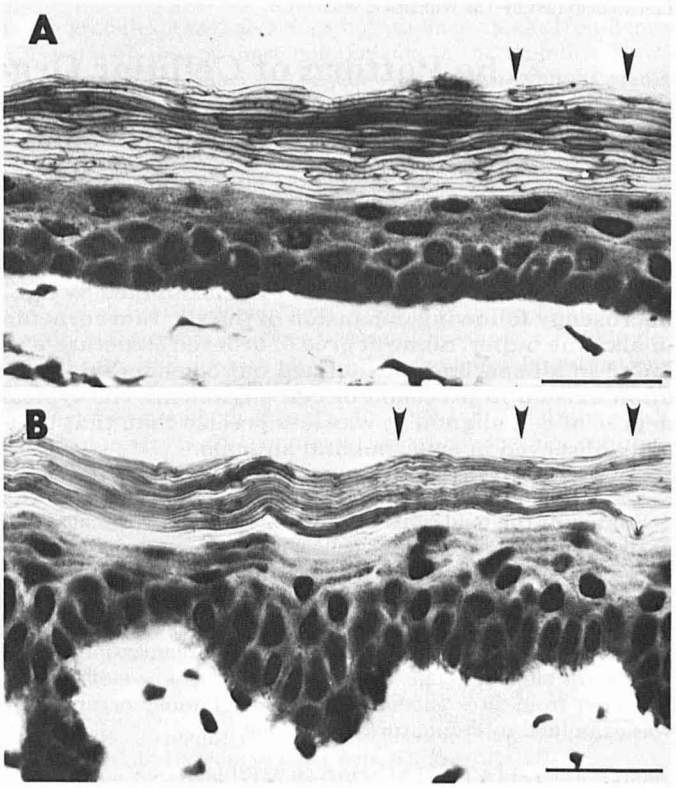

FIG 2. *A*. Specimen illustrating least appearance of ordered structure observed. Runs of 3–4 irregularly aligned cells are commonly seen and longer runs (basal part of stratum corneum beneath arrows) are occasionally seen. Scalp, 47-yr-old male *B*, Specimen showing alignment of 3–4 layers of nucleated cells beneath the two stratum corneum columns marked by *arrows*. Thoracic skin from 67-yr-old male (*scale* = 30 μm).

palmar [4] and oral mucosal [12] surfaces in man has been noted. The samples of human epidermis examined in the present study were taken only from regions which, in the light of previous work, would be expected to form cell columns. The presence of some degree of cell alignment in all of the specimens examined indicates that in man, as in other species, a columnar pattern of organization is typical of the greater part of the epidermis.

Two differences concerning the organization of the human stratum corneum were observed. First, none of the human specimens examined showed a degree of precision of cell alignment comparable to that which has been regularly observed in other species. Secondly, quite a large variation in the degree of precision of cell alignment was observed from specimen to specimen. This variation in the degree of cell alignment could not be consistently correlated to the age or sex of the donor or to the anatomical region from which the specimen was taken.

A lack of a clear alignment of stratum granulosum cells was the typical finding for human specimens. However, in some specimens (e.g., Fig 2*B*) alignment of 3–4 layers of nucleated cells similar to that seen in rodents and the rhesus monkey (Fig 3) was apparent. The typical absence of a marked discernable alignment of these strata in human tissue may, in part, be related to the less orderly pattern of the tissue as a whole but it seems probable from the general appearance of the tissues that cell flattening and alignment may occur at a relatively later stage of cell maturation in man.

The presence of a columnar pattern of organization in the epidermis has been associated with a relatively low rate of cell replacement. For example, in the specialized regions that normally do not show such a pattern the rate of cell replacement is relatively high [2,11,13,14]. Furthermore, the columnar pattern normally present elsewhere in the epidermis is disturbed when rates of cell proliferation are raised by experimental manipulation [15,16]. Menton and Eisen [5] have shown the absence of cell columns from human epidermis involved in pathological processes which raise the rate of cell proliferation. There is evidence that, in some regions, the columnar structure in the epidermis of rodents may be in an unstable state [13], possibly because the rate of cell production is close to the upper limit which permits establishment of minimum surface relationships [17]. It may thus be that the irregularity of cell alignment typical of normal human skin is associated with a higher rate of cell replacement than rodent epidermis: the data available for rates of cell production in human epidermis are limited but those reviewed by Potten [18] suggest that the daily rate of cell formation per columnar unit may be twice as high in man as in the mouse.

If the degree of organization of the stratum corneum is related to rates of cell proliferation, factors such as stress or surface abrasion, which have been shown to affect cell proliferation in experimental animals [19,20] would be expected to lead to variation with subject or region. It was anticipated that some consistent variation of the structure of the stratum corneum might be found either in relation to a record of stress, (for

TABLE I. *Results of grading each specimen for cell alignment*[a]

	Age Sex	3 Days F	3 mo M	32 yr M	46 yr M	47 yr M	47 yr F	50 yr M	67 yr M	67 yr F	71 yr M
Organization of *Stratum Corneum*											
Abdomen		2.8	3.0	2.4	2.0	2.0	2.8	3.0	2.8	3.0	2.4
Arm		3.0	2.8	2.8	3.0	2.0	2.8	2.8	2.6	2.8	2.4
Chest		2.0	3.0	3.0	3.0	3.0	2.2	3.0	2.8	3.0	2.2
Scalp		3.0	2.8	2.8	2.8	1.8	2.8	2.6	1.8	2.2	2.8
Organization of *Stratum Granulosum*											
Abdomen		2.0	3.0	2.6	1.8	2.6	2.0	3.0	2.6	2.0	3.0
Arm		3.0	3.0	2.6	2.4	3.0	2.2	3.0	2.4	2.0	3.0
Chest		1.8	2.2	3.0	2.2	2.6	2.0	3.0	3.0	2.8	3.0
Scalp		2.8	3.0	1.8	2.0	1.8	3.0	3.0	2.0	2.8	2.0

[a] Each grade recorded in the table represents the mean of the grades recorded (see text) for 5 or more sections on each specimen. A considerable variation was observed in the regularity of alignment of cells in the stratum corneum and stratum granulosum from specimen to specimen but all specimens presented evidence of some degree of ordered structure.

example in the form of severe chronic illness prior to death), or regional or age variations, which might be related to surface environmental insults or different rates of cell proliferation. This was not observed but the number of subjects examined in the present study was perhaps too small to lead to a high probability that such causes of variation could be identified. It appears that further studies to investigate the relationship of such factors to the structure of human epidermis would be worthwhile.

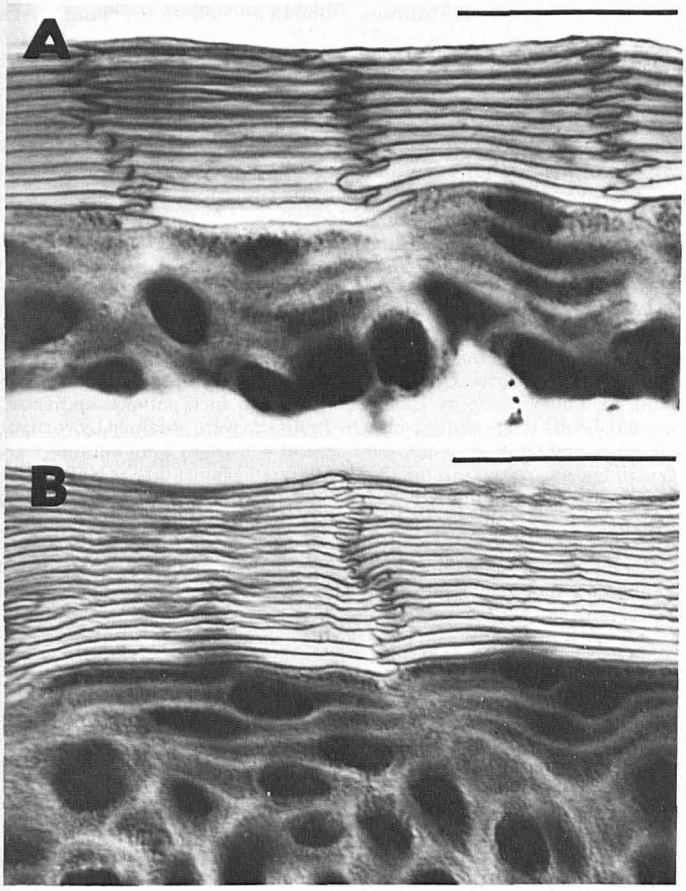

FIG 3. *A*, Hamster ear skin. *B*, Rhesus monkey thoracic skin. Both specimens show regular, vertically-aligned, interdigitations between cells of adjacent columns in the stratum corneum. Several layers of nucleated cells are aligned beneath the stratum corneum columns (*scale* = 30 μm).

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